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Short Communication

Immunization in the First Month of Life may Explain Decline in Incidence of IDDM in The Netherlands

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A low cumulative incidence of IDDM was reported in Dutch males born in 1962 (*Diabetologia* 1992: 35: 139–142) compared to males born in previous or later years. The cause for the decreased risk has not been previously explained. We propose that children born in 1962 during an European smallpox epidemic may have received the smallpox vaccine in the first month of life and this may have attributed to the decreased risk of IDDM in these children. We have shown that immunization with several different vaccines starting in the first month of life prevents diabetes in NOD mice and BB rats (*Autoimmunity* 1996: 24: 137–145) while immunization at birth with the BCG vaccine is associated with an decreased risk of IDDM in humans (*Infectious Diseases in Clinical Practice* 1997: 6: 449–454). An even bigger decline in diabetes is seen in rodents and associated in humans when one compares immunization starting in the first month of life to immunization starting after 2 months, since the later has been associated with an increased risk of IDDM. Immunization studies in the past have typically followed patients for only several weeks to determine any unplanned affects on autoimmune disease. Due to the potential benefit of reducing the incidence of diabetes by 50% through age 18 we believe clinical trials are warranted to study the effect of timing of immunization on IDDM.

Keywords: Diabetes mellitus, Insulin-dependent, Vaccination, BCG vaccine, Immunization schedule, Human

Epidemiology data shows that in the cumulative incidence of diabetes up to the age of 18 differed significantly in Dutch male birth cohorts.[1] There were two significant drops in the incidence of diabetes, one was centered around 1962 when the cumulative incidence dropped to 1.1 per 1000 ($P < 0.05$), and the other was centered around 1966 when the cumulative incidence dropped to 1.71 per 1000.

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TABLE I Cumulative incidence of type I diabetes mellitus in dutch military recruits, age 18

Year of birth	No. of type I diabetics	Cumulative incidence diabetes per 1000	*P* value	Smallpox cases Western Europe	Doses smallpox Vaccine, Europe
1960	189	1.85		1	Data not available
1961	167	1.76		79	167
1962	96	1.11	$P < 0.05$	51	235
1963	188	1.5		28	175
1964	198	1.83		0	110
1965	203	1.93		1	107
1966	184	1.71	N.S.	72	110
1967	219	2.07		4	112
1968	194	1.96		2	117
1969	264	2.11		0	Data not available
1970	234	2.12		22	Data not available

Spearman rank correlation coefficient test: $0.05 > P > 0.025$; Refs. [1,4,5].

The drops are in contrast to a cumulative incidence of diabetes outside of these troughs of about 1.98 per 1000 (Table I). The drops in 1962 and 1966 both occurred during smallpox epidemics in Europe and can be explained by immunization of newborn infants in these periods with smallpox vaccine.

Western Europe had major epidemics of smallpox centered around the years 1962 and 1966. The epidemic in 1962 actually started in 1961 continuing into 1963 and included 158 cases from 7 western European countries.[4] The 1966 epidemic included 72 cases and was limited to the United Kingdom. There was a strong emphasis placed on vaccination during the smallpox epidemic of 1961–1963 as demonstrated by World Health Organization statistics showing 23.5 million Europeans were vaccinated with the smallpox vaccine in 1962 compared to an norm of about 11 million in nonepidemic years.[5] Changes in smallpox vaccine acceptance were detected around 1962 and 1966 in the Netherlands[6] however this was not reflected by an increased immunization rate in the rest of Europe possibly because many countries had just finished extensive immunization campaigns a few years earlier.

It was customary at the time for physicians practicing in areas with a low incidence of smallpox to wait until the patient was several months old before administering the smallpox vaccine, however in areas with a high incidence of smallpox, like third world countries, smallpox vaccine was often given at birth.[7,8] The common practice in the Netherlands in the 1960s was to immunize children with the smallpox vaccine starting at 2 months of age in normal, nonepidemic conditions.[9] Given the fact that the vaccine literature recommends immunization earlier than usual in times of epidemics, it would have been expected that a number of physicians would have given the vaccine several weeks earlier, as in 4 weeks of age or at birth. The resulting switch in immunization can explain the drop in the incidence of IDDM in the cohorts born during smallpox epidemics. The approximately 50% decrease in the incidence of IDDM by age 18 which occurred could be expected if the smallpox vaccine was given on average 3 weeks earlier because human BCG data indicates immunization starting after 2 month of life is associated with an increased risk of IDDM while immunization starting at birth is associated with a decreased risk of IDDM.[3]

Immunization records were not kept so the per cent of people born in 1962 who were immunized prior to 2 months could not be determined, furthermore we could not determine the immunization status of diabetics and controls. Diabetes data was also not available on women from the Netherlands or on other Europeans born during the smallpox epidemics. Immunization studies in the past have typically followed patients for only several weeks to determine any unplanned affects on autoimmune

disease. Due to the potential benefit of reducing the incidence of diabetes by 50% through age 18 we believe clinical trials are warranted to study the effect of timing of immunization on IDDM.

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